1: Hum Gene Ther. 2008 Mar;19(3):229-40.

Protective immunity against neu-positive carcinomas elicited by electroporation of plasmids encoding decreasing fragments of rat neu extracellular domain.

Rolla S, Marchini C, Malinarich S, Quaglino E, Lanzardo S, Montani M, Iezzi M, Angeletti M, Ramadori G, Forni G, Cavallo F, Amici A.

Molecular Biotechnology Center, Dipartimento di Scienze Cliniche e Biologiche, University of Turin, 10123 Turin, Italy.

We have shown that electroporation of plasmid carrying extracellular and transmembrane domains (EC-TM plasmid) encoded by the rat neu oncogene triggers a protective immune response toward rat p185(neu)-positive tumors in both wild-type BALB/c mice and cancer-prone rat neu-transgenic BALB-neuT mice. To identify the critical fragments that confer this protective immunity, mice were electroporated with plasmids encoding the TM domain associated with decreasing fragments of the EC domain and the antitumor protection afforded, the titer of antibody, and cytotoxic T lymphocyte (CTL) activity elicited to Neu protein were evaluated. Plasmids encoding EC fragments shortened by 70 (EC1-TM plasmid), 150 (EC2-TM), 230 (EC3-TM), 310 (EC4-TM), and 390 (EC5-TM) NH(2)-terminal residues afforded effective protection. Plasmids encoding shorter truncated proteins were ineffective. When the immunogenic protein was retained in the cytoplasm (EC1-TM, EC2-TM, and EC5-TM), only a CTL response was elicited, whereas when it was also expressed on the membrane (EC4-TM) both CTLs and antibodies were induced. EC4-TM encoding a truncated protein with an EC portion of only 344 amino acids conferred protection on both BALB/c and BALB-neuT mice comparable to that of EC-TM.

PMID: 18269312 [PubMed - indexed for MEDLINE]